**PATENT** 

Attorney Docket No.: VOSS1130

In re Application of: Peltonen et al.

Application No.: 09/509,595

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Amendments to the Specification

Please replace the paragraph starting at page 2, line 14, with the following amended paragraph:

Please replace the paragraph starting on page 19, line 11, with the following amended paragraph:

B) The genomic structure of the APGD1 gene. The 14 true exons of the gene are compared with the gene models predicted with different gene finding programs (Uberbacher, E., et al., *Proc. Natl. Acad. Sci, USA*, **88**, 11261-11265 (1991); Thomas, A., & Skolnick, M. H., *IMA J. Math. Appl. Med. Biol.*, **11**, 149-160 (1994); Kulp, D., et al., ISMB-96, St. Louis, MO, AAAI/MIT Press. available on the worldwide web at hgc.lbl.gov/projects/genie.html) (1996)). Solid boxes indicate exons in which at least one boundary was correctly predicted, open boxes are false exons. Genomic sequence of cosmid clones Q21D1, Q22G11, EST matches, detailed gene prediction data and the intron-exon boundaries of APGD1 are available at http://ehr21.rz-berlin.mpg.de/APECED.html/ on the internet at chr21.rz-berlin.mpg.de.

Please replace the paragraph starting on page 23, line 30, with the following amended paragraph:

We have mapped APECED to chromosome 21q22.3 by linkage analysis and further refined the localization by linkage disequilibrium to a region between the markers D21S25 and D21S171 (Aaltonen, J., et al., Nature Genet, 8, 83-87 (1994); Aaltonen et al., Genome Research 7 (1997), 820-827). This critical region was 350 kb in size and a bacterial clone contig was constructed across this region. Several techniques were used to identify candidate genes in this gene rich region. Exon trapping (Buckler, A., et al., *Proc. Natl. Acad. Sci., USA*, 88, 4005-4009, (1991)) and cDNA selection (Lovett, M., et al., *Proc. Natl. Acad. Sci., USA*, 88, 9628-9632, (1991)) methods identified a new gene, 694N10 (Accession No. Z93322), just distal to the previously known PFKL gene (Phosphofructokinase of liver type, EC 2.7.1.11)

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(Elson et al., Genomics, 7, 47-56 (1990)) (Figure 1A). Partial unordered genomic sequence encompassing the PFKL gene (available at the International Chromosome 21 genomic sequence repository, on the worldwide web at eri.uchsc.edu http://www-eri.uchsc.edu/chr21/eridna.html) was used to generate a new polymorphic marker, PB1. This marker showed an obligatory recombination in one APECED family, thus we were able to restrict the APECED region to 145 kb between the markers D21S25 and PB1 (Figure 1A). Therefore 694N10 was excluded as causative gene for APECED.

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Please replace the Abstract on page 49, with the following amended Abstract: The present invention relates to a nucleic acid molecule encoding a (poly)peptide cosegregating in mutated form with Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dystrophy (APECED). In addition, the invention relates to a mammalian, preferably murine, homologue of the above nucleic acid molecule. The present invention further relates to a nucleic acid molecule deviating by at least one mutation from the nucleic acid molecule described above wherein said mutation co-segregates with APECED and is an insertion, a deletion, a substitution and/or an inversion, and wherein said mutation further results in a loss or a gain of function of the (poly)peptide encoded by said mutated nucleic acid molecule. Furthermore, the present invention relates to a vector comprising the nucleic acid molecules described above and to a host transformed with said vector. In addition, the present invention relates to a process of recombinantly producing a (poly)peptide encoded by the nucleic acid molecules described above comprising culturing or raising said host and isolating said (poly)peptide from said culture or said host. The present invention further relates to the (poly)peptide encoded by said nucleic acid molecules or produced by the process described above. Additionally, the present invention relates to an antibody that specifically recognizes said (poly)peptides. Moreover, the present invention relates to a method for testing for a carriership for APECED or for a corresponding disease state comprising testing a sample obtained from a prospective patient or from a person suspected of carrying a predisposition for a mutation in the wild type nucleic acid molecule described above or a mutated form of the

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(poly)peptide encoded by said mutated nucleic acid molecule in an immuno-assay using the antibody described above.

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